

**REMARKS**

In response to the Examiner's comments and to expedite prosecution applicants have canceled claims 22-25 and 27-28. Applicants have canceled these claims without prejudice and without waiver of their right to file for and obtain claims directed to any canceled subject matter in divisional and continuing applications which claim priority from this application.

Applicants have amended claim 21 to recite the subject matter of the elected invention. Applicants have amended claim 21 to recite a method for inducing angiogenesis in a mammal comprising the step of administering an effective amount of a homodimeric OP-1 or an amino acid sequence variant thereof.

Applicants have amended claim 26 and 29 to properly depend from claim 21.

None of these amendments adds new matter.

Applicants now address the Examiner's objection and rejections.

**THE OBJECTIONS**

Claim 27

The Examiner has objected to claim 27 for reciting BMP-5, BMP-6, BMP-8, GDF-6 and GDF-7, which are drawn to non-elected groups.

Applicants have canceled claim 27 and amended claim 21 to recite a method for inducing angiogenesis in a mammal homodimeric OP-1 or a variant thereof. Accordingly, the Examiner's objection has been obviated.

**THE REJECTIONS**

35 U.S.C. § 112, First Paragraph - Claim 27

The Examiner has rejected claim 27 under 35 U.S.C. § 112, first paragraph for lack of written description. The Examiner contends that the specification only provides written description for a dimeric species of OP-1 and not for amino acid sequence variants of OP-1. Applicants traverse.

Applicants respectfully submit that the specification provides adequate written description for variants of OP-1. The specification at page 17, lines 8-16 describes that variants include those containing sequences that share at least 70% amino acid homology with the C-terminal seven cysteine domain of hOP-1. In addition, the

specification clearly describes what is intended by 70% amino acid sequence homology (see specification page 17, line 26 to page 20, line 2). Accordingly, applicants request that the Examiner withdraw this written description rejection.

35 U.S.C. § 102(b)

Eriksson, et al. - Claims 21, 26 and 29

The Examiner has rejected claims 21, 26 and 29 under 35 U.S.C. § 102(b) as being anticipated by Eriksson et al., U.S. patent 5,840,693 ("Eriksson"). The Examiner contends that the specification does not limit what is included or excluded as a morphogenic protein and that Eriksson teaches VEGF-B. The Examiner further contends that Eriksson teaches that VEGF-B may be used to accelerate angiogenesis and that it may be produced by the expression of a recombinant DNA molecule in a host. Applicants traverse.

Amended claim 21 and claims dependent thereon recite a method for inducing angiogenesis in a mammal comprising the step of administering an effective amount of a homodimeric OP-1 or a variant thereof.

As the Examiner has stated, Eriksson discloses VEGF-B and its uses. Eriksson does not disclose a method of inducing angiogenesis using a homodimeric OP-1 or variant

thereof, and therefore, does not anticipate the claims of the instant application. Accordingly, applicants request that the Examiner withdraw this rejection.

Connolly et al. - Claims 21, 26 and 29

The Examiner has rejected claims 21, 26 and 29 under U.S.C. § 102(b) as being anticipated by Connolly et al., U.S. patent 5,008,196 ("Connolly"). The Examiner contends that Connolly teaches a morphogenic protein wherein the protein comprises a disulfide bonded dimeric species and that the morphogenic protein can be used to stimulate endothelial cell growth. The Examiner further contends that Connolly teaches that the morphogenic protein is produced by expression of recombinant DNA in a host cell. Applicants traverse.

As described above, the amended claims recite a method of inducing angiogenesis in a mammal comprising the step of administering an effective amount of a homodimeric OP-1 or a variant thereof. Connolly discloses vascular permeability factor and a method for stimulating endothelial cell growth. Connolly does not disclose a method for inducing angiogenesis with a homodimeric OP-1 or a variant thereof. Therefore, Connolly does not anticipate the claims

of the instant application. Accordingly, applicants request that the Examiner withdraw this rejection.

Israel, et al. - Claims 21 and 26-29

The Examiner has rejected claims 21 and 26-29 under U.S.C. § 102(b) as being anticipated by Israel et al., WO93/09220 ("Israel"). The Examiner contends that Israel teaches recombinant expression of morphogenic proteins in host cells including disulfide bonded dimeric BMP-7. The Examiner further contends that Israel teaches that the heterodimeric proteins are capable of stimulating the growth of bone forming cells, inducing differentiation of progenitor cells of the bone-forming cells and increasing neuronal activity. The Examiner contends that although Israel does not characterize the BMP-7 as angiogenic, the claimed functional limitation would be an inherent property.

Applicants traverse.

First, applicants have canceled claims 27 and 28, thus, obviating the rejection with respect to those claims.

Second, as described above, amended claim 21 and claims dependent therefrom recite a method of inducing angiogenesis comprising the step of administering a homodimeric OP-1 or amino acid variant thereof.

Israel merely discloses the use of heterodimeric BMP-7 for treating bone defects and wound healing. Israel does not disclose a method of inducing angiogenesis comprising the step of administering a heterodimeric OP-1 or amino acid variant thereof. Accordingly, Israel does not anticipate the amended claims of the instant application. Applicants request that the Examiner withdraw this rejection.

**CONCLUSION**

For all the above reasons, applicants request that the Examiner withdraw all outstanding rejections and allow the pending claims.

The Examiner is invited to telephone applicants' representatives regarding any matter that may be handled by telephone to expedite allowance of the pending claims.

Respectfully submitted,



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